UNITED STATES DEPARTMENT OF COMMERCE United States Patent and Trademark Office Address: COMMISSIONER FOR PATENTS P.O. Rev. 1450

EXAMINER

P O Box 1450 Alexandria, Virgima 22313-1450 www.usplo.gov

NOTICE OF ALLOWANCE AND FEE(S) DUE

30623 7590 07722/2010 MINTZ, LEVIN, COHN, FERRIS, GLOVSKY AND POPEO, P.C

HAVLIN, ROBERT H
ART UNIT PAPER NUMBER

ONE FINANCIAL CENTER BOSTON, MA 02111

1626 DATE MAILED: 07/22/2010

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/786,710 | 02/24/2004 | Mark L. Nelson | 16534-512C01US | 3651 |

TITLE OF INVENTION: 7-AND 9- CARBAMATE, UREA, THIOUREA, THIOCARBAMATE, AND HETEROARYL-AMINO SUBSTITUTED TETRACYCLINE COMPOUNDS

| APPLN. TYPE | SMALL ENTITY | ISSUE FEE DUE | PUBLICATION FEE DUE | PREV. PAID ISSUE FEE | TOTAL FEE(S) DUE | DATE DUE |
|----------------|--------------|---------------|---------------------|----------------------|------------------|------------|
| nonprovisional | NO | \$1510 | \$300 | \$0 | \$1810 | 10/22/2010 |

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 1SI. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FIEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail Mail Stop ISSUE FEE Commissioner for Patents 1.0. Box 1430 periods 22313-144

Alexandria, Virginia 22313-1450 or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address and indicated unless corrected below of directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or EFEE ADDRESS' for maintenance fee notifications Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address) papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission. 30623 7590 07/22/2010 Certificate of Mailing or Transmission MINTZ. LEVIN, COHN, FERRIS, GLOVSKY AND POPEO, P.C1 hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sulficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPIO (571) 273-2885, on the date indicated below. ONE FINANCIAL CENTER BOSTON, MA 02111 (Depositor's name (Signature APPLICATION NO. FILING DATE FIRST NAMED INVENTOR ATTORNEY DOCKET NO. CONFIRMATION NO 10/786.710 02/24/2004 Mark L. Nelson 16534-512C01US 3651 TITLE OF INVENTION: 7-AND 9- CARBAMATE, UREA, THIOUREA, THIOCARBAMATE, AND HETEROARYL-AMINO SUBSTITUTED TETRACYCLINE COMPOUNDS APPLN, TYPE SMALL ENTITY ISSUE FEE DUE PUBLICATION FEE DUE PREV. PAID ISSUE FEE TOTAL FEE(S) DUE DATE DUE nonprovisional NO \$1510 \$300 \$0 \$1810 10/22/2010 EXAMINER ART UNIT CLASS-SUBCLASS 548-400000 HAVLIN, ROBERT H 1626 Change of correspondence address or indication of "Fee Address" (37 CFR 1.363). 2. For printing on the patent front page, list (I) the names of up to 3 registered patent attorneys or agents OR, alternatively, Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached. (2) the name of a single firm (having as a member a "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. Use of a Customer registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is Number is required. listed, no name will be printed. 3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment. (A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY) Please check the appropriate assignee category or categories (will not be printed on the patent): 🔲 Individual 🚨 Corporation or other private group entity 📮 Government 4a. The following fee(s) are submitted: 4b. Payment of Fee(s): (Please first reapply any previously paid issue fee shown above) ☐ Issue Fee A check is enclosed. ☐ Publication Fee (No small entity discount permitted) Payment by credit card. Form PTO-2038 is attached. The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number (enclose an extra copy of this for Advance Order - # of Copies (enclose an extra copy of this form). 5. Change in Entity Status (from status indicated above) □ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2). a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27. NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office. Authorized Signature _ Date

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| ONE FINANCIA | | ART UNIT | PAPER NUMBER | | |
| BOSTON, MA 0 | 2111 | 1626 | | | |

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)

(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 0 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 0 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

Application No. Applicant(s) 10/786,710 NELSON ET AL. Notice of Allowability Examiner Art Unit ROBERT HAVLIN 1626 -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS. This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308. This communication is responsive to 6/24/2010. 2. X The allowed claim(s) is/are 1,4,6,7,9-11,13,14,19,21,23-26,30,32,34-40,56-65,67,68,82,103-107,109-112 and 117-138. 3. Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f). a) \square All b) ☐ Some* c) ☐ None of the: 1. T Certified copies of the priority documents have been received. 2. Certified copies of the priority documents have been received in Application No. 3. Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)). * Certified copies not received: _____. Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. THIS THREE-MONTH PERIOD IS NOT EXTENDABLE. A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient. CORRECTED DRAWINGS (as "replacement sheets") must be submitted. (a) Including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached 1) hereto or 2) to Paper No./Mail Date (b) including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d). 6. DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL. Attachment(s) 1. Notice of References Cited (PTO-892) 5. Notice of Informal Patent Application 2. Notice of Draftperson's Patent Drawing Review (PTO-948) Interview Summary (PTO-413), Paper No./Mail Date Information Disclosure Statements (PTO/SB/08). 7. X Examiner's Amendment/Comment Paper No./Mail Date 4. T Examiner's Comment Regarding Requirement for Deposit 8. X Examiner's Statement of Reasons for Allowance of Biological Material 9. ☐ Other .

/Robert Havlin/ Examiner, Art Unit 1626 Application/Control Number: 10/786,710 Page 2

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EXAMINER'S AMENDMENT

 An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Chris Olson on 7/9/10.

The application has been amended as follows:

Cancel claims 108, 139-143, 145-147, and 149-158.

2. The following is an examiner's statement of reasons for allowance:

In view of applicant's remarks the examiner has reconsidered the 35 USC 112 first - enablement rejection and decided to withdraw the rejection. As applicant points out, the development of tetracycline antibiotic compounds has been well studied, including related derivatives such as applicant claims. Furthermore, the enabling disclosure teaches methods of how to make and test the compounds for the relevant activity in a manner that supports the claims. Because the remaining ground of rejection was withdrawn, the previously withdrawn claims are hereby rejoined and allowed. The closest prior art is that of Hlavka et al. (US RE40,183) which teaches a genus of compounds of the following formula:

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$$\begin{array}{c|c} X & NCH_{3)2} \\ \hline \\ RNH & OH & OH \\ \hline \\ OH & OH \\ \end{array}$$

Although part of the instant claim scope is encompassed by the Hlavka reference, such as in col. 141 where "n=0" in the definition of "R", one of ordinary skill in the art is not sufficiently taught by the prior art how to select the subgenus of the instant claims such that the instant claims are obvious over the prior art. Thus, the above "R" variable and "X" variables differ from the instant claims in a non-obvious manner.

3. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT HAVLIN whose telephone number is (571)272-9066. The examiner can normally be reached on Mon. - Fri., 7:30am-5pm FST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joe McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert Havlin/ Examiner, Art Unit 1626